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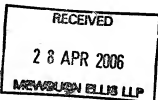
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DUE	24/10/06	ENT'D FOR	
ENT'D	22/10/06	SMW	
TO 1	Reference	SMW	5566155

Date	26-04-2006
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Applicant/Proprietor
Abaron Biosciences, Inc.

Application No./Patent No.
00936281.5 - 1223

Summons to attend oral proceedings pursuant to Rule 71(1) EPC

You are hereby summoned to attend oral proceedings arranged in connection with the above-mentioned European patent application.

The matters to be discussed are set out in the communication accompanying this summons (EPO Form 2906).

The oral proceedings, which will not be public, will take place before the examining division

on 24.10.06 at 10.00 hrs in Room ~~4C.10~~ ^{6C.10 (LP C1015)} EPO
Rijswijk, Patentlaan 2, NL-2288 EE Rijswijk (ZH)

No changes to the date of the oral proceedings can be made, except on serious grounds (see OJ EPO 10/2000, 456).

If you do not appear as summoned, the oral proceedings may continue without you (R. 71(2) EPC). Your attention is drawn to Rule 2 EPC, regarding the language of the oral proceedings, and to the OJ EPO 9/1991, 489, concerning the filing of authorisations for company employees and lawyers acting as representatives before the EPO.

The final date for making written submissions and/or amendments (Rule 71a EPC), is 22.09.06.

You are requested to report in good time beforehand to the porter in the EPO foyer. Room _____ is available as waiting room.

Parking is available free of charge in the underground car park (see map enclosed).

1st Examiner:
Tuyman A

2nd Member:
Vanhalst K

Chairman:
Van Der Kooij M

For the Examining Division

Annexes:
Confirmation of receipt (Form 2936)
Communication (EPO Form 2906)



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The examination is being carried out on the **following application documents**:

Description, Pages

1-26 as originally filed

Claims, Numbers

1-34 received on 29.01.2002 with letter of 24.01.2002

Drawings, Sheets

1/8-8/8 as originally filed

Reference is made to the following documents cited on the search report; the numbering will be adhered to in the rest of the procedure:

D12: SCUDDER P R ET AL.: BIOCHIMICA ET BIOPHYSICA ACTA, vol. 660, no. 1, 1981, pages 128-135.

In addition the following documents (D) are cited by the examiner (see the Guidelines, C-VI, 8.7). Copies of the documents are annexed to the communication and the numbering will be adhered to in the rest of the procedure:

D13: ICHIKAWA, Y ET AL.: J.AM.CHEM.SOC., vol. 114, 1992, pages 9283-9298.

D14: WONG, C-H. ET AL.: J.AM.CHEM.SOC., vol. 114, 1992, pages 7321-7322.

D15: QIAO, L. ET AL.: J.AM.CHEM.SOC., no. 118, 1996, pages 7653-7662.

D16: CHATTERJEE, S.: INDIAN JOURNAL OF BIOCHEMISTRY & BIOPHYSICS, vol. 34, 1997, pages 56-60.

D17: TAKAYAMA, S ET AL.: BIOORGANIC & MEDICINAL CHEMISTRY, vol. 7, 1999, pages 401-409.

D18: BROQUET, P ET AL.: JOURNAL OF NEUROCHEMISTRY, vol. 54, no. 2, 1990, pages 388-394.

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- 1 The applicant has requested Oral Proceedings in the reply letter of 24.01.06. Thus the Examining Division herewith summons the applicant to attend Oral Proceedings pursuant to Article 116(1) EPC in view of the above mentioned request for Oral Proceedings. The proceedings are to be held on the date indicated on the cover page.

Preamble:

The present application is very seriously flawed with respect to the requirements of the EPC.

In the search report numerous documents have been cited that take away the novelty and/or inventive step of the vast majority of the claims as originally filed. It is the impression of the examining division that the applicant tries to find the gaps in a field, where already a lot of research has been done. Patenting was designed for protecting the factual results of successful research as reward for making available concrete technical results to the public, not for reserving unexplored parts of research (see T278/00: point 6). Indeed, in fact the present application is an extremely broadly drafted research programme, covering a large part of research already known to the person skilled in the art, with NO proven factual contribution in the application as originally filed. As such the claims are certainly not commensurate with the contribution of the present application. Now the applicant has submitted with the letter of 24.01.06 some technical factual results that correspond to some of the embodiments as a selection from a great number of possibilities evoked in the description. The applicant has had more than five years to come with evidence that there are embodiments that actually work and limited the claims accordingly. This is not allowable under Article 83 EPC (see T0609/02: point 8). Although formally the examining division cannot object to the present limitation under Article 123(2) EPC, the gist of this Article is, that the public should not be taken by surprise. Since it was not possible to predict which of the embodiments of the application as originally filed would be workable embodiments, by granting the current application the public would yet be subject to surprise. This is not fair to the public. An additional search was carried out to focus on the subjects that have been elected for examination. Additional documents were found that take away the novelty and/or inventive step of the present claims.

The objections in the light of these documents and some of the documents indicated on the search report are so serious that on basis of the present claims the examining division

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is contemplating refusing the application, as will be explained hereunder. However, in view of the introduction of new documents, the examining division has decided to set the date of oral proceedings at about 6 months from the issuing of this communication so as to give the applicant sufficient time to formulate arguments.

The Examining Division considers that the application does not meet the requirements of Article 54,56,83,84 and 123(2) EPC.

- 2 The amendments filed with the letter dated 24.01.06 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 123(2) EPC. The amendments concerned are the following:
 - 2.1 Claims 7 and 25 mention "FucT-II". No basis could be found for this enzyme throughout the application as originally filed. Therefore the content of these claims extends beyond the application as originally filed.
- 3 The application does not meet the requirements of Article 84 EPC, because the subject matter of claims 1-39 is neither clear nor supported nor sufficiently disclosed over the whole scope claimed (Article 83 EPC).
 - 3.1 Present claims 1-39 relate to compounds or the use of such compounds defined by reference to a desirable characteristic or property, namely compounds being non-carbohydrate compounds that mimic the hydrophobic structure of a sugar recognised by a glycosyltransferase (fucosyltransferase in claims 1-10 and 24-39). An attempt is made to define the compound by reference to a result to be achieved. In fact the above mentioned feature used to define the solution to the problem is the problem itself. It is unclear from the wording of the claims which compounds still would fall within the scope of the claim, and which compounds would not. In the absence of any teaching at the date of filing as to the **three dimensional structure** or other detailed structural information of the active site of the enzymes mentioned in these claims, the person skilled in the art was unable to figure out at the date of filing whether a compound would fall within the scope of the claims. The definition given in the description (page 3, line 31-page 4, line 2 in combination with page 6, lines 1-22, page 8 line 4, page 9, line 8) is so broad that the only way to figure out whether a



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compound fits this definition would amount to using the screening protocol of claims 11-23: This is considered to be an **undue burden**. The compounds are allowed to have hydrophilic substituents (page 6, lines 1-22, page 9, lines 4-7). Some vague remarks about the hydrophobicity constant on page 8, lines 12-27 are not of much guidance either. It is unclear to what degree a compound is supposed to be hydrophobic to mimic the hydrophobic structure of a sugar ie. to fit the scope of the claims. Therefore, the claims are so unclear and lack support to such an extent that the requirements of Article 84 EPC are not met.

- 3.2 Present claims 1-10 and 24-39 are so-called "**reach-through**" claims and **must** be deleted. The examining division will be intransigent with respect to these claims.

Present claims 1-10 and 24-39 relate to compounds or the use of such compounds defined by reference to a desirable characteristic or property, namely compounds being non-carbohydrate compounds that mimic the hydrophobic structure of a sugar recognised by a fucosyltransferase.

The claims cover all compounds having this characteristic or property, whereas the application provides **neither support** within the meaning of Article 84 EPC **nor disclosure** within the meaning of Article 83 EPC for such compounds. Therefore, the claims lack support, and the application lacks disclosure. To select such compounds via a method used in claims 11-23, would require undue experimentation and therefore this claim is not allowable (Guidelines C-III, 4.7). Independent of the above reasoning, the claims also lack clarity (Article 84 EPC). An attempt is made to define the compound by reference to a result to be achieved. These claims will therefore be excluded from the examination as to novelty and inventive step. Note that the "experimental information" provided with the letter of 24.01.06 is irrelevant for the assessment of support and disclosure for these claims; this information will only be taken into account for claims 11-23.

- 3.3 The term "non-carbohydrate compounds" used in the claims is not clear. The description furthermore casts doubt on the scope of the claims by including "amino sugars" (ie. aza sugars) in the definition of sugars (carbohydrate compounds). Therefore, the definition of non-carbohydrate compounds used in the description is different from what the person skilled in the art would understand: For

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a person skilled in the art aza sugars, which do not have the characteristic of anomery are non-carbohydrate compounds. Therefore, the claims are not clear from the wording of the claims alone.

- 3.4 In the rest of the present communication under the term "non-carbohydrate compounds that mimic the hydrophobic structure of a sugar recognised by a glycosyltransferase" any compound will be understood that does not have one or more saccharide units: an aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols, due to the lack of clarity mentioned in items 3.1-3.3.
- 4 The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 11-13,16-18 is not new in the sense of Article 54(1) and (2) EPC.
- 4.1 D12 discloses a method of inhibiting a fucosyltransferase, the method comprising contacting the fucosyltransferase in vitro with a non-carbohydrate compound (p-chloromercuribenzoate), that mimics the hydrophobic structure of a sugar recognised by the fucosyltransferase.
- The method disclosed in D12 also can be considered as a method of identifying a fucosyltransferase inhibitor, the method comprising contacting the fucosyltransferase, an acceptor substrate, and a donor substrate with a non-carbohydrate test compound that mimics the hydrophobic structure of a sugar recognized by the fucosyltransferase and determining the degree to which the activity of the fucosyltransferase is inhibited in the presence of the test compound. (D12, abstract; page 129, right-hand column, 2nd paragraph in combination with page 130, left-hand column, last paragraph-right-hand column, line 12).

Therefore D12 anticipates the subject matter of independent claim 11.

- 4.2 D13 discloses a method of inhibiting a fucosyltransferase, the method comprising contacting the fucosyltransferase in vitro with a non-carbohydrate compound (D13, Table III: compounds 8-10,12,13), that mimics the hydrophobic structure of a sugar recognised by the fucosyltransferase.

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The method disclosed in D13 also can be considered as a method of identifying a fucosyltransferase inhibitor, the method comprising contacting the fucosyltransferase, an acceptor substrate, and a donor substrate with a non-carbohydrate test compound that mimics the hydrophobic structure of a sugar recognized by the fucosyltransferase and determining the degree to which the activity of the fucosyltransferase is inhibited in the presence of the test compound. (D13, abstract; Table III: compounds 8-10, 12, 13; page 9285, left-hand column, lines 2-18; page 9296, right-hand column, last paragraph-page 9297, 1st line). It is mentioned *in expressis verbis* in D13 that the substrates bind in such a way to have a hydrophobic face on one side (abstract; page 9295, left-hand column, lines 5-11). Therefore in as far as claim 11 can be understood, these disclosures perfectly fall under the scope of this claim.

- 4.3 D14 (Table I) and D15 (Table 1, compounds 1, 16 and 17; page 7662 paragraph: "synergistic inhibition") disclose similar subject matter and also anticipate independent claim 11. Moreover D14 shows a possible complex of the aza sugar in the active site of the fucosyltransferase in which drawing it is clear that the hydrophilic groups are positioned below the plane of the "envelope structure" (which is a stable conformation) and that above the plane of the envelope the molecules substituents are essentially hydrophobic. (see also D15, figure 3). Therefore in as far as claim 11 can be understood, these disclosures perfectly fall under the scope of this claim.
- 4.4 D16 discloses a screening assay for inhibitors of galactosyltransferases (abstract) in which inter alia non-carbohydrate compounds (D-PDMP) are incubated with the enzyme to determine the degree of inhibition. These molecules are no longer amino sugars and **certainly** can be considered as non-carbohydrate compounds that mimic the hydrophobic structure of a sugar recognised by the galactosyltransferase. Therefore in as far as claim 11 can be understood, this disclosure perfectly falls under the scope of this claim.
- 4.5 D17 discloses a screening assay for inhibitors of galactosyltransferases (abstract) in which inter alia non-carbohydrate compounds (figure 3, molecules 1-4; page 407, left-hand column, 3rd full paragraph-right-hand column line 5; page 407-408:



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bridging paragraph) are incubated with the enzyme to determine the degree of inhibition. These molecules are no longer amino sugars and **certainly** can be considered as non-carbohydrate compounds that mimic the hydrophobic structure of a sugar recognised by the galactosyltransferase. Therefore in as far as claim 11 can be understood, this disclosure perfectly falls under the scope of this claim.

- 4.6 D18 discloses a screening assay for inhibitors of sialyltransferases (abstract) in which inter alia non-carbohydrate compounds (N-(6-aminohexyl)-5-chloro-1-naphthalenesulfonamide; desipramine) are incubated with the enzyme to determine the degree of inhibition. These molecules are no longer amino sugars and **certainly** can be considered as non-carbohydrate compounds that mimic the hydrophobic structure of a sugar recognised by the sialyltransferase. Therefore in as far as claim 11 can be understood, this disclosure perfectly falls under the scope of this claim.
- 5 The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 11-23 does not involve an inventive step in the sense of Article 56 EPC.
- 5.1 A *conditio sine qua non* for the recognition of inventive step (Article 56 EPC) of a claim is that a solution to the problem posed in the claim is provided. If the inventive step of a claimed invention is based on a given technical effect, the latter should, in principle, be achievable over the whole area claimed (T939/92). As this is not the case here since the achievement of the desired technical effect has been shown in the additional evidence filed with the letter of 21.01.06 only for some specific compounds in combination with some specific enzymes, but not over the whole scope claimed (see 5.2) inventive step must be denied.
- 5.2 The subject matter of present claim 11-22 is seriously flawed with respect to Article 56 EPC, because it does not provide a solution over the whole scope claimed. D13 discloses that the non-carbohydrate compound deoxynojirimycin is a substrate for the galactosyltransferase b1,4GalT and not an inhibitor. Therefore simply to inhibit a galactosyltransferase with just any non-carbohydrate compound will not always provide a solution to the problem posed. The guidance as to which compound to



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select for the screening protocol is therefore insufficient.

- 5.3 Independent claim 11 is manifestly not novel and can therefore not be inventive either.

Dependent claims 12-23 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the EPC with respect to novelty and/or inventive step, the reasons being as follows:

The incorporation of the features of claims 12-23 into independent-claim 11 is either known or obvious from D12-D18 or falls within the knowledge and ability of a person skilled in the art.

- 6 If for claims 11-23 the above mentioned objections can be overcome, the application will be considered to lack unity within the meaning of Article 82 EPC for the following reasons:

The problem to be solved in the present application (PA) relates to the provision of inhibitors of glycosyltransferase activity, in which a monosaccharide is transferred from a donor nucleotide sugar to a sugar molecule attached to an acceptor substrate being a glycolipid or glycoprotein. The single general concept which can be identified a priori as linking the various claimed inventions and which forms a solution to the above mentioned problem relates to "non-carbohydrate compounds as inhibitors for the above mentioned class of glycosyltransferases"

However, D12-D18 disclose such compounds as inhibitors for such enzymes.

In the light of D12-D18, each document if taken alone, the above identified single general concept is not novel and inventive and can thus not be the single general inventive concept as required by Article 82 EPC and Rule 30 EPC. The present application can then therefore be considered not to fulfill the requirement of unity as laid down in Article 82 EPC.

Consequently the groups of inventions will then be split up as follows:

Methods for providing inhibitors of glycosyltransferase activity, in which a monosaccharide is transferred from a donor nucleotide sugar to a sugar molecule

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attached to an acceptor substrate being a glycolipid or glycoprotein, in which the glycosyltransferase is:

- 1) fucosyltransferase
- 2) galactosyltransferase
- 3) sialyltransferase
- 4) N-acetylglucosaminyltransferase

No other technical features could be identified that form a technical relationship among each of the separate inventions claimed and which could be considered as special technical feature within the meaning of Rule 30(1) EPC.

In this case applicant will be asked to state upon which invention further prosecution of this application should be based and to limit the application accordingly. Other inventions are to be excised from the claims, description and drawings if any.

- 7 The excess subject-matter relating to a possible in vivo/therapeutical use of the inhibitors (description page 3, lines 19-22) should be deleted, since it is in contradiction with the scope of the claims (Article 84 EPC, GCIII, 4.3a). This type of subject-matter is excluded from patentability under Article 52(4) EPC, since it involves a method of treatment of the human or animal body.
- 8 For the above reasons, the Examining Division is contemplating to refuse the present application based on the claims on file (Article 97(1) EPC).
- 9 The applicant is reminded to respect the limit date of Rule 71a, if he decides to submit in writing documents and accordingly adapted claims, overcoming the outstanding objections.
- 9.1 It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 29(1) EPC. The applicant should also indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.



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- 9.2 In order to facilitate the examination of the conformity of the amended application with the requirements of Article 123(2) EPC, the applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based.

If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

- 9.3 When filing amended claims the applicant should at the same time bring the description into conformity with the amended claims. Care should be taken during revision, especially of the introductory portion and any statements of problem or advantage, not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).
- 9.4 To meet the requirements of Rule 27(1)(b) EPC, the documents D1-D18 should be identified in the description and the relevant background art disclosed therein should be briefly discussed.